Comorbidities associated with COVID-19 mortality: A retrospective study in an intermediate care facility in Cape Town, South Africa

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Background. The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic continues to place a significant burden on healthcare systems across the globe. Previous studies have shown that patients with comorbidities who contract SARS-CoV-2 develop more severe COVID-19 disease and are at a higher risk of mortality. However, literature in the intermediate care setting is limited.
Objectives. To evaluate the association between comorbidity and mortality in the intermediate care setting.
Methods. A retrospective observational study was performed at Brackengate Intermediate Care Facility (BICF), a 330-bed field hospital, during the second wave of COVID-19 in Cape Town, South Africa. Data of all adult patients admitted from 1 November 2020 to 28 February 2021 who met the inclusion criteria were analysed. Data were obtained from electronic hospital patient administration systems. Comparisons were made using χ^2 or Fisher's exact testing with a 5% level of confidence used to determine significance. Logistic regression models were used to investigate the independent association between clinical variables of interest and overall mortality.
Results. A total of 2 508 patients were analysed, of whom 2 476 (98.7%) were laboratory confirmed cases of COVID-19. The median number of admissions per day was 14. The mean age was 58 years, and 1 449 (57.8%) were female. The most prevalent comorbidities were hypertension (62.6%), diabetes (46.9%) and obesity (28.0%), while 8.0% of patients were HIV-positive. The overall mortality was 13.3% (333/2 508). Patients with at least one comorbidity were 1.4 times more likely to die (odds ratio (OR) 2.4; 95% confidence interval (CI) 1.6 - 3.5), and this risk increased significantly with cumulative comorbidities. Patients who required >40% oxygen were at 5.5 (95% CI 4.3 - 7.1) times higher mortality risk. Variables independently associated with mortality were age >60 years, FiO_2 >40%, previous cerebrovascular accident, concurrent tuberculosis infection and chronic kidney disease.
Conclusion. Patients with comorbidities are at an increased risk of death in COVID-19 disease, and should be monitored closely. Oxygen requirement >40% is also associated with a higher likelihood of dying. Intermediate care facilities can provide valuable relief to acute care facilities by admitting high-risk patients for closer monitoring and management.

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The pandemic of the novel coronavirus infectious disease (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has had a global impact.

Various risk factors have been associated with mortality in patients diagnosed with COVID-19. Worldwide research has highlighted advanced age and patients with hypertension, diabetes mellitus, coronary heart disease, chronic obstructive pulmonary disease, obesity and chronic kidney disease at increased risk of mortality.[1-4] Advanced age has been shown to pose the strongest risk factor for mortality.[2] The South African (SA) population has a high prevalence of non-communicable diseases and is therefore at high risk of severe disease and mortality. In addition, SA has a high burden of disease resulting from communicable diseases such as HIV/AIDS and tuberculosis.[5]

SA studies reflect results found internationally, and broaden our understanding of the impact COVID has had on developing countries. In a large cohort study on COVID-related in-hospital mortality in SA (*N*=219 265), the most prevalent comorbidities were hypertension (38.6%), diabetes (29.0%) and HIV (11.7%).[6] In another study, a large proportion (60%, *n*=372) of deceased patients had diabetes mellitus, with almost half of them having a haemoglobin A1c (HbA1c) >9%. A HbA1c >7% is suboptimal in diabetic patients on treatment. Mortality was significantly lower in diabetic patients with a HbA1c <7%.[7] SA research further

indicated that HIV infection is associated with an increased risk of mortality (adjusted odds ratio (aOR) 1.34; 95% confidence interval (CI) 1.27 - 1.43). Patients living with HIV not on antiretroviral therapy (ART) were also more likely to die compared with patients on ART (aOR 1.45; 95% CI 1.22 - 1.72).[6]

Although specific comorbidities place people at higher mortality risk, the number of comorbidities also seems to be associated with a poorer outcome.[8] In a Chinese study,[8] patients with one comorbidity had a hazard ratio of 1.79 (95% CI 1.16 – 2.77), and this increased to 2.59 (95% CI 1.61 - 4.17) for patients with more than one comorbidity.

Intermediate care in our setting is acute care provided to stable patients who are still too unwell to be treated at home or at another health facility.[9] Brackengate Intermediate Care Facility (BICF) opened in July 2020 as part of the Western Cape Province's response to the COVID-19 pandemic. BICF would assist in taking a significant patient load from overworked hospitals, allowing them to have open beds for new patients. BICF functions as a step-down facility and provides intermediate care to stable COVID-19 patients who require hospitalisation for ongoing supplementary oxygen and management of their comorbidities.

Minimal data are available from intermediate care facilities in SA for COVID-19. Recent publications from intermediate care facilities in SA either broadly describe their data and experience or are focused on specific comorbidities.[10,11] No data are available regarding the association between comorbidities and mortality in an intermediate care facility, and whether SA's unique disease profile plays a role in the outcome. Therefore, the present study will fill the knowledge gap pertaining to the epidemiological profile of patients with COVID-19 managed at intermediate care facilities. The primary objective of the study was to determine the association between comorbidities and mortality in COVID-19 patients hospitalised in an intermediate care facility in Cape Town, SA. A secondary objective was to describe the workload and epidemiological profile of patients admitted to the BICF.

Methods

Study design

A retrospective observational study was performed. Approval was obtained from the University of Cape Town Human Research Ethics Committee (ref. no. 502/2020) as well as the Western Cape Department of Health Research Committee.

Study setting

BICF is a state-funded 330-bed field hospital that accepts patients diagnosed with COVID-19 who require further in-hospital care. The drainage area includes the Cape Town Metropole, Cape Winelands and Overberg health districts. The admission criteria for BICF are given in the appendix (https://www.samedical.org/file/1866). The majority of patients are referred from acute hospitals in the Cape Town metropolitan area and come from low-income areas and informal settlements. BICF is a step-down facility and provides intermediate care to COVID-19 patients who require hospitalisation for supplementary oxygen and/or the treatment of their comorbidities (only patients who have had their initial triage, stabilisation and work-up performed at their base hospital are accepted). There is an oxygen port at each bed, with eight beds fitted to provide high-flow nasal oxygen ($HFNO_2$). There is one ventilator available which can be utilised when patients require intubation and ventilation before being transferred to a facility with an intensive care unit (ICU).

Patients whose condition improves and who are successfully weaned off oxygen are either discharged home or to an isolation facility. Patients who deteriorate are assessed for $HFNO_2$ and ICU using the critical care triage tool.[12] Palliative care is initiated for patients deemed not eligible.

Study population

All adult patients (≥18 years) hospitalised in BICF for COVID-19 from 1 November 2020 to 28 February 2021 were included. This time period correlated with the second peak of COVID-19 infections in SA. Convenience sampling was used, and all patients meeting the admission criteria (appendix) were eligible.

Data collection and management

The list of patients admitted to BICF during the study period was obtained from the electronic hospital patient administration system. Data were extracted from the hospital's electronic medical records using patients' folder numbers. Laboratory results were obtained from the National Health Laboratory Service web portal. Each folder number was assigned a unique study number. Data were directly entered into a password-protected Excel (Microsoft, USA) spreadsheet. Once the data had been collected, all folder numbers were deleted.

A standardised data collection sheet was used, and all data collectors were trained to ensure reliable data. Multiple electronic administration resources were used to retrieve patient information to ensure data were accurate. This included electronic inpatient notes, online discharge summaries and National Health Laboratory Service (NHLS) test results.

COVID-19 infection was defined as laboratory-confirmed (polymerase chain reaction (PCR) positive or rapid antigen positive) or 'clinical COVID' (suggestive clinical and radiological findings in patients with a negative or inconclusive PCR test). Chronic lung disease only included interstitial lung disease and post-tuberculous structural lung disease. Obesity was subjectively assessed by the treating clinician.

Statistical analysis

Summary statistics were used to describe all variables. Categorical data were summarised using frequency counts, percentages or proportions, and distributions of variables were presented as two-way tables or bar charts. Medians or means were used as the measures of central tendency for continuous responses, and standard deviations or quartiles as indicators of spread. Independent proportions were compared using the *t*-test or the Mann-Whitney U test. The relationship between categorical variables was determined using the χ^2 test or Fisher's exact test. The relationships between continuous variables were analysed using appropriate analysis of variance (ANOVA) tests or the Kruskal-Wallis test if the data did not

meet the requirements for a parametric test. Logistic regressions models were used to investigate the independent association between clinical variables of interest and overall mortality. A 5% level of confidence was used to determine significance. Data were analysed using SPSS Statistics for Windows, Version 27.0 (IBM Corp., USA).

Results

A total of 2 552 patients were admitted to BICF during the study period, of whom 44 were excluded (COVID-19 negative *n*=43, aged <18 years *n*=1). The 43 COVID-19-negative patients were admitted during the early stages of the second wave as patients under investigation (PUIs); COVID-19 was subsequently excluded. Therefore 2 508 patients were included in the analyses. Three patients who were transferred out from Brackengate had missing transfer outcome data, and were excluded from the relevant analyses. One patient had missing highest oxygen requirement data.

The median (25th - 75th percentile) number of admissions per day was 14 (5 - 38), and peaked towards the end of December 2020, with a maximum of 60 admissions per day on 29 December 2020 and 12 January 2021. The number of admissions corresponded to the trend of new infections registered in the Western Cape during the same time period (median of 806 per day, maximum 4 241 on 31 December 2021) (Fig. 1). Patients were admitted to BICF from 18 different public healthcare facilities across the Cape Town metropolitan area; the highest numbers of patients were received from Tygerberg Hospital (*n*=391, 15.6%), Karl Bremer Hospital (*n*=310, 12.4%) and Eerste River Hospital (*n*=303, 12.1%). Fifty (2.0%) patients were admitted directly from home or general practitioners via telemedicine consultations (Table 1).

From the 2 508 patients analysed, the majority (*n*=2 476, 98.7%) were laboratory-confirmed cases of COVID-19, and 1 449 (57.8%) were female. The mean (standard deviation) age was 58 (13.6) years, and patients who died were significantly older than those who survived (67.6 years v. 56.6 years, $p<0.001$) (Table 2). Almost all patients (2 402/2 507, 95.8%) received some form of oxygen supplementation and ventilatory support during the study (at any facility) with a significant difference between those who died v. survived ($p<0.001$). The median (25th - 75th percentile) length of stay at BICF was 5 (3 - 9) days. Most patients (*n*=2 116, 84.4%) were discharged home, 292 (11.6%) died and 100 (4.0%) were transferred to other healthcare facilities. Of those transferred, 75 (75.0%) were for escalation of care, and 78 (78.0%) were transferred to Tygerberg Hospital, the closest tertiary facility. A further 41 (41.0%) of the 100 patients transferred died, and 33 (33.0%) were transferred back to BICF. The overall mortality was therefore 13.3% (*n*=333; unknown *n*=3, 0.1%).

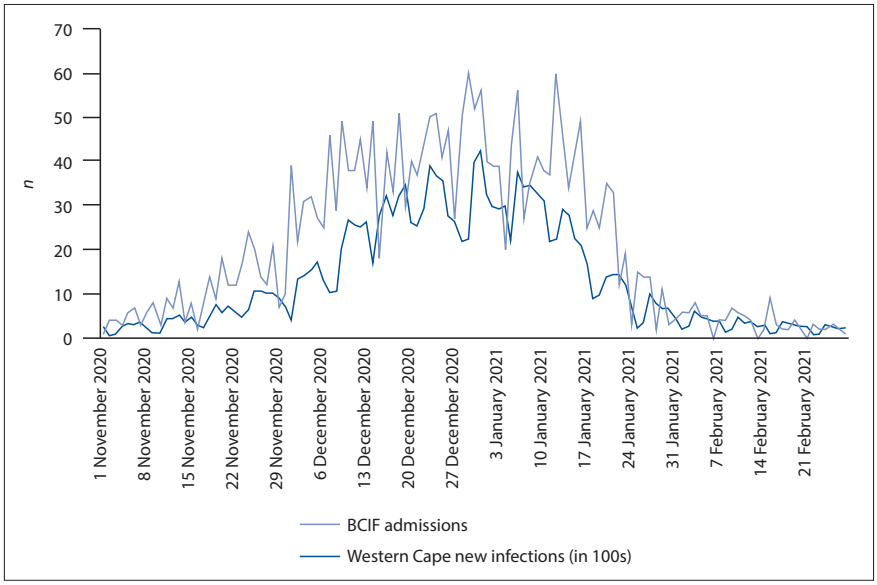

Fig. 1. Number of daily admissions to Brackengate Intermediate Care Facility (BCIF), and corresponding numbers of new COVID-19 infections in the Western Cape Province (in 100s).

Table 1. Facilities across the Cape Town Metropole (*n*=21) from which COVID-19 patients were admitted to Brackengate Intermediate Care Facility (*N*=2 508)

Referring facility	Patients, *n* (%)
Tygerberg Hospital	391 (15.6)
Karl Bremer Hospital	310 (12.4)
Eerste River Hospital	303 (12.1)
New Somerset Hospital	259 (10.3)
Mitchell's Plain Hospital	224 (8.9)
Khayelitsha Hospital	208 (8.3)
Helderberg Hospital	202 (8.1)
Groote Schuur Hospital	169 (6.7)
Victoria Hospital	149 (5.9)
Wesfleur Hospital	100 (4.0)
False Bay Hospital	59 (2.4)
Telemedicine consultations*	50 (2.0)
Heideveld Hospital	28 (1.1)
Worcester Hospital	21 (0.8)
Stikland Hospital	14 (0.6)
Caledon Hospital	8 (0.3)
Clanwilliam Hospital	4 (0.2)
Elsies River Hospital	3 (0.1)
Private healthcare*	3 (0.1)
Paarl Hospital	2 (0.1)
Alta du Toit Aftercare Centre	1 (<0.1)

*Includes more than one referral centre.

Table 2. Demographics and clinical characteristics of study population (*N*=2 508), overall and per mortality outcome (unknown mortality *n*=3)

Characteristic	All (*N*=2 508), *n* (%)*	Alive (*n*=2 172), *n* (%)*	Died (*n*=333), *n* (%)*	*p*-value
Sex				
Male†	1 059 (42.2)	901 (41.5)	155 (46.5)	0.081
Female	1 449 (57.8)	1 271 (58.5)	178 (53.5)	
Age (years), mean (SD)	58 (13.6)	56.6 (13.3)	67.6 (11.6)	<0.001
COVID-19 diagnosis				
Laboratory confirmed†	2 476 (98.7)	2 141 (98.6)	332 (99.7)	0.113
Clinical diagnosis	32 (1.3)	31 (1.4)	1 (0.3)	
Highest oxygen and ventilation requirements (at any facility)				
Unknown	1	-	1	<0.001
None (room air)	102 (4.1)	98 (4.5)	4 (1.2)	
Nasal prongs	751 (29.9)	737 (33.9)	14 (4.2)	
Face mask	476 (18.9)	470 (21.6)	6 (1.8)	
Non-rebreather mask	760 (30.3)	598 (27.5)	162 (48.6)	
Double-barrel oxygen‡	202 (8.1)	105 (4.8)	95 (28.5)	
CPAP therapy	5 (0.2)	4 (0.2)	1 (0.3)	
HFNO§	198 (7.9)	153 (7.0)	44 (13.2)	
Intubated and ventilated	13 (0.5)	7 (0.3)	6 (1.8)	
Received HFNO at BICF				
Yes§	52 (26.3)	15 (9.8)	36 (81.8)	<0.001
No	146 (73.7)	138 (90.2)	8 (18.2)	
Initial disposition from BICF				
Discharged home	2 116 (84.4)	2 116 (97.4)	0 (0.0)	<0.001
Death	292 (11.6)	0 (0.0)	292 (87.7)	
Transferred†	100 (4.0)	56 (2.6)	41 (12.3)	
Length of stay (days), median (25th - 75th percentile)	5 (3 - 9)	5 (3 - 9)	5 (2 - 9)	0.782

SD = standard deviation; CPAP = continuous positive airway pressure; HFNO = high-flow nasal oxygen; BICF = Brackengate Intermediate Care Facility.
*Unless otherwise specified. †Outcome unknown *n*=3. ‡Outcome unknown *n*=2. §Outcome unknown *n*=1.

The most prevalent comorbidities among the study patients were hypertension (*n*=1 569, 62.6%), diabetes (*n*=1 176, 46.9%) and obesity (*n*=702, 28.0%), while 201 (8.0%) were HIV-positive. Hypertension, chronic kidney impairment, ischaemic heart disease, heart failure, previous cerebrovascular accident (CVA) and dementia were associated with mortality (Table 3). HIV-positive patients with a CD4 cell count <200/mm^3 were at a higher risk of death (OR 2.75; 95% CI 1.05 - 7.24).

A total of 2 046 (81.6%) patients had at least one comorbidity and were 1.4 times more likely to die than those who had no comorbidities (OR 2.4; 95% CI 1.6 - 3.5). Patients with only one comorbidity were associated with a 90% increased risk of mortality (OR 1.9; 95% CI 1.3 - 2.9). Risk of mortality increased with incremental additional comorbidities (Table 4).

Patients who received any percentage of supplementary oxygen were 3.88 (95% CI 1.42 - 10.60) times more likely to die than those only breathing room air. Patients who required >40% oxygen were 5.53 (95% CI 4.30 - 7.11) times at higher mortality risk than those on room air or receiving <40% oxygen. In patients who received oxygen, those who needed >40% were 21.44 (95% CI 13.53 - 33.98) times more likely to die. The risk of mortality increased as concentration of oxygen increased; the odds of mortality in those receiving >40% were 8.70 (95% CI 3.18 - 23.85) times higher than those who received no oxygen supplementation (Table 5).

Univariable associations between mortality and comorbidities are presented as ORs with 95% CI (Table 6). Variables independently associated with mortality were age ≥60 years (aOR 3.77; 95% CI 2.85 - 4.99), >40% oxygen required (aOR 6.53; 95% CI 4.95 - 8.56), previous CVA (aOR 2.42; 95% CI 1.8 - 4.23), current tuberculosis (aOR 4.70; 95% CI 1.65 - 13.41) and chronic kidney impairment (aOR 2.52; 95% CI 1.74 - 3.64) (Table 7).

Discussion

This is the first study in SA from a COVID-19 field hospital looking at a range of comorbidities associated with mortality during the second wave of the COVID-19 pandemic. The results from our cohort suggest that advanced age (>60 years), hypertension, chronic kidney disease, heart failure, ischaemic heart disease, previous CVA, dementia, chronic obstructive pulmonary disease and HIV (CD4 <200/mm^3) were risk factors associated with mortality. A multivariate analysis of the data revealed that advanced age (>60 years), current tuberculosis and previous CVA were independently associated with death. Patients receiving 40% oxygen and more were also associated with higher mortality. The risk for mortality increased with every additional comorbidity.

The in-hospital mortality rate at BICF during the second COVID-19 peak (11.6%) was lower than the total in-hospital mortality in SA (23.0%) between 5 March 2020 and 27 March 2021.[6] An

Table 3. Comorbidities present in patients admitted to BICF (*N*=2 508), 1 November 2020 - 28 February 2021 (unknown mortality *n*=3)

Comorbidity	All, *n* (%)*	Alive (*n*=2 172), *n* (%)*	Died (*n*=333), *n* (%)*	*p*-value
Hypertension	1 569 (62.6)	1 325 (61.02)	242 (72.7)	<0.001
Diabetes	1 176 (46.9)	1 003 (46.2)	171 (51.4)	0.078
Haemoglobin A1C (median (Q1 - Q3))	7.9 (6.5-10.5)	8.0 (6.5-10.6)	7.7 (6.6-9.8)	0.332
Haemoglobin A1C ≥7% (*n*=1 399)	892 (63.8%)	767 (64.2)	125 (61.3)	0.424
Obesity	702 (28.0)	618 (28.5)	84 (25.2)	0.222
Pre-diabetic	234 (9.3)	201 (9.3)	33 (9.9)	0.702
HIV	201 (8.0)	180 (8.3)	21 (6.3)	0.215
On anti-viral therapy	158 (78.6)	142 (70.6)	16 (8.0)	0.781
CD4 cell count (median (Q1 - Q3))	290 (151 - 451)	295 (159 - 458)	154 (66 - 390)	0.646
CD4 cell count <200/mm^3 (*n*=181)	116 (64.1%)	108 (66.7)	8 (42.1)	0.035
Chronic kidney impairment	194 (7.7)	136 (6.3)	58 (17.4)	<0.001
eGFR (median (Q1-Q3))	41 (31-49)	41 (32-48)	42 (28-51)	0.731
eGFR <30 mL/min (*n*=194)	46 (23.7)	29 (21.3)	17 (29.3)	0.231
COPD	141 (5.6)	114 (5.2)	27 (8.1)	0.035
Ischaemic heart disease	127 (5.1)	100 (4.6)	27 (8.1)	0.007
Heart failure	109 (4.3)	86 (4.0)	23 (6.9)	0.014
Asthma	89 (3.5)	81 (3.7)	8 (2.4)	0.223
Previous cerebrovascular accident	76 (3.0)	54 (2.5)	22 (6.6)	<0.001
Chronic lung disease	40 (1.6)	31 (1.4)	9 (2.7)	0.084
Malignancy	40 (1.6)	31 (1.4)	9 (2.7)	0.084
Auto-immune disorders	37 (1.5)	34 (1.6)	3 (0.9)	0.468
Dementia	36 (1.4)	24 (1.12)	12 (3.6)	0.002
Current tuberculosis	22 (0.9)	16 (0.7)	6 (1.8)	0.061
Any comorbidity	2 046 (81.6)	1 742 (80.2)	302 (90.7)	<0.001
>1 comorbidity	993 (39.6)	819 (37.7)	174 (52.3)	<0.001

BICF = Brackengate Intermediate Care Facility; Q1 - Q3: 25th - 75th percentile; eGFR = estimated glomerular filtration rate; COPD = chronic obstructive pulmonary disease.
*Unless otherwise specified.

Table 4. Association between number of comorbidities and risk of death in COVID-19 patients admitted to BICF over the study period

Comorbidities, *n*	Patients, *n* (%)	OR (95% CI)	*p*-value
0	462 (18.4)	Reference	Reference
1	1 053 (42.0)	1.9 (1.3 - 2.9)	0.002
2	716 (28.5)	2.7 (1.8 - 4.0)	<0.001
3	216 (8.6)	3.5 (2.2 - 5.8)	<0.001
4	54 (2.2)	4.4 (2.1 - 9.1)	<0.001
5	7 (0.3)	5.5 (1.0 - 29.8)	0.046

BICF = Brackengate Intermediate Care Facility; OR = odds ratio; CI = confidence interval.

explanation for this substantial difference could be that BICF only accepted patients who were referred from acute hospitals after they were diagnosed and stabilised. Patients with high and/or increasing oxygen requirements were managed at acute hospitals unless they were admitted for palliative care. Similarly, patients who qualified for high care/ICU were transferred out if their oxygen requirements increased.

Advanced age predicted mortality with an OR of 3.8; this is consistent with global data that have indicated that elderly populations have more severe disease and therefore are at increased risk of mortality.[1,3,4,13] SARS-CoV-2, as with other viruses, is cleared by the T-cell response, which may be impaired in the elderly.[3] This, along with the increased production of type 2 cytokines, may render patients prone to acute respiratory distress syndrome and severe disease, as well as mortality.[1,3] Those of advanced age are also more likely to have comorbid illnesses, which independently increase mortality risk.

Cerebrovascular disease and chronic kidney disease have previously been shown to be associated with increased mortality.[1,3,4,13] Both are the result of target organ damage due to cardiovascular disease such as hypertension, which was also found to be associated alone with poor outcomes in COVID-19. The mechanisms for the development of severe disease in patients with established cardiovascular disease are not completely understood, but have been attributed to endothelial dysfunction and dysregulation of the renin angiotensin aldosterone system (RAS).[3] The receptor for SARS-CoV-2, angiotensin-converting enzyme 2 (ACE2), is mainly expressed in the lung epithelium, as well as in blood vessels.[13]

Table 5. Association between oxygen requirements and mortality in patients admitted to BICF with COVID-19

Oxygen requirement	Alive, *n*	Dead, *n*	OR (95% CI)
Any supplemental oxygen required v. room air			
Room air	98	4	3.88 (1.42 - 10.60)
Supplemental oxygen required*	2 074	328	
FiO_2 0.4 split (all patients)			
Room air and FiO_2 ≤0.4	1 902	186	5.53 (4.30 - 7.11)
FiO_2 >0.4	27	146	
FiO_2 0.4 split (only patients receiving oxygen)			
FiO_2 ≤0.4	1 207	20	21.44 (13.53 - 33.98)
FiO_2 >0.4	867	308	
Incremental oxygen use (all patients)			
Room air	98	4	Reference
FiO_2 ≤0.4	1 207	20	0.41 (0.14 - 1.21)
FiO_2 >0.4	867	308	8.70 (3.18 - 23.85)

BICF = Brackengate Intermediate Care Facility; OR = odds ratio; CI = confidence interval, FiO_2 = fraction of inspired oxygen.
*Includes all patients who required supplemental oxygen, including patients who were on room air but then needed oxygen at a later stage.

Table 6. Univariable associations between mortality and comorbidities in patients admitted to BICF for COVID-19

Predictor variable	B	SE	*p*-value	OR (95% CI)	–2 log likelihood
Gender (male)	–0.206	0.118	0.082	0.08 (0.81 - 0.65)	1 960.536
Age (≥60 years)	1.332	0.132	0.000	3.79 (2.93 - 4.91)	1 948.156
Oxygen requirement (any FiO^2)	1.354	0.514	0.008	3.88 (1.42 - 10.6)	1 948.895
Oxygen requirement (FiO^2 ≥0.4)	1.710	0.128	0.000	5.53 (4.3 - 7.11)	1 793.661
Diabetes	0.207	0.118	0.079	1.23 (0.98 - 1.56)	1 960.456
Diabetes (non and HbA1c ≤7% combined)	0.051	0.123	0.679	1.05 (0.83 - 1.34)	1 963.381
Hypertension	0.531	0.131	0.000	1.7 (1.32 - 2.2)	1 946.099
Dementia	1.208	0.359	0.001	3.35 (1.66 - 6.76)	1 953.921
Previous cerebrovascular accident	1.020	0.260	0.000	2.78 (1.67 - 4.32)	1 950.304
Obesity	–0.165	0.135	0.222	0.848 (0.65 - 1.11)	1 962.033
HIV-positive	–0.295	0.238	0.217	0.75 (0.47 - 1.19)	1 961.921
HIV (negative and CD4 ≥200 combined)	–0.754	0.371	0.042	0.47 (0.23 - 0.97)	1 958.478
Current tuberculosis	0.905	0.482	0.061	2.47 (0.96 - 6.36)	1 960.521
Heart failure	0.588	0.243	0.015	1.8 (1.12 - 2.9)	1 958.264
Ischaemic heart disease	0.603	0.225	0.007	1.83 (1.18 - 2.84)	1 957.095
Chronic kidney impairment	1.150	0.169	0.000	3.16 (2.27 - 4.4)	1 923.336
COPD	0.466	0.223	0.037	1.59 (1.03 - 2.46)	1 959.533
Asthma	–0.453	0.375	0.227	0.635 (0.3 - 1.33)	1 961.911
Other chronic lung disease	0.652	0.383	0.089	1.92 (0.91 - 4.07)	1 960.991
Malignancy	0.652	0.383	0.089	1.92 (0.91 - 4.07)	1 960.991
Auto-immune disorders	-0.559	0.605	0.355	0.57 (0.18 - 1.87)	1 962.556

BICF = Brackengate Intermediate Care Facility; SE = standard error; OR = odds ratio; CI = confidence interval; FiO_2 = fraction of inspired oxygen; COPD = chronic obstructive pulmonary disease.

Table 7. Independent mortality predictors in patients admitted to BICF with COVID-19

Multivariate associations	B	SE	*p*-value	aOR (95% CI)	–2 log likelihood
Age (≥60 years)	1.328	0.143	<0.001	3.77 (2.85 - 4.99)	1 635.288
Oxygen requirement (FiO_2 ≥0.4)	1.876	0.138	<0.001	6.53 (4.98 - 8.56)	
Previous cerebrovascular accident	0.884	0.285	<0.001	2.42 (1.38 - 4.23)	
Current tuberculosis	1.548	0.535	<0.001	4.70 (1.65 - 13.41)	
Chronic kidney impairment	0.923	0.188	<0.001	2.52 (1.74 - 3.64)	

BICF = Brackengate Intermediate Care Facility; SE = standard error; aOR = adjusted odds ratio; CI = confidence interval, FiO_2 = fraction of inspired oxygen.

It is speculated that depletion of ACE2 in COVID-19 could lead to decreased down-regulation of the RAS system and therefore increase susceptibility to pulmonary oedema or congestive cardiac failure and fatal outcomes.[1,13]

A concerning finding was that patients with current tuberculosis were also independently associated with an

increased mortality risk (aOR 4.7). The likelihood of co-infection is high in our population, as tuberculosis is highly prevalent in the Western Cape Province (up to 1 026 per 100 000 individuals had bacteriologically confirmed tuberculosis in 2018).[14] Conflicting results have emerged from studies evaluating the mortality of patients with a dual diagnosis of tuberculosis and COVID-19. One recent meta-analysis, however, found a significant association between mortality in patients diagnosed with tuberculosis and COVID-19 (OR1.94, 95% CI 1.28 - 2.93).[15] The ACE2 receptor is again implicated, with expression being increased during tuberculosis coinfection, leading to exacerbation of COVID-19.[16] It is also speculated that COVID-19 may enhance progression of tuberculosis, leading to increased mortality from tuberculosis in co-infected patients.[16]

An unexpected and important finding was that diabetes was not associated with higher mortality even though the number of diabetic patients seen during the second wave outnumbers the prevalence of diabetes in SA by more than threefold. This adds to the findings of another Cape Town-based COVID-19 field hospital, which showed a relatively low mortality rate (6%) in hospitalised patients with diabetes.[10] Another unexpected finding was that a raised HbA1c did not increase the risk of mortality in diabetic patients. We speculate that this may be the result of good in-hospital blood glucose control using sliding scales, and close adjustment of intermediate- and long-acting insulin, leading to improved outcomes. The prevalence of diabetes among our study population (47%) is suggestive that patients with diabetes are a high-risk population requiring close monitoring. Perhaps further research can be done into the effects of glucose control on COVID-19 outcomes in an intermediate care setting.

Our study indicated that having any comorbidity, regardless of which, increased the risk of mortality substantially with an incremental number of comorbidities. This is in keeping with other studies and can be attributed again to endothelial dysfunction, RAS dysregulation and immunocompromise associated with chronic disease.[1,3,4,13]

Patients requiring any supplemental oxygen were associated with increased mortality, and requiring >40% of inspired oxygen during admission was the strongest predictor of mortality (aOR 6.5). Although not a comorbidity, requiring a higher concentration of oxygen is an indicator of severe disease, and therefore mortality is expected to increase.

Our study had several limitations. An observational study has inherent bias, but this was limited by using well-defined inclusion criteria. Secondly, patients were not consistently weighed when admitted, therefore obesity was likely to be under-reported. HbA1c tests were only performed for known diabetic patients and patients in whom diabetes was suspected. It is, however, possible that patients with HbA1c >6.0 were missed, as not all patients admitted to BICF had HbA1c on the NHLS web portal. Caution should be taken to generalise the results as our study population included patients from a single intermediate care facility situated in a unique health setting.

Conclusion

It is evident that patients with comorbidities, including but not limited to cardiovascular disease and its complications, advanced HIV and tuberculosis co-infection, as well as those of advanced age, are at increased risk of severe COVID-19 disease and mortality. These patients should be monitored more closely, and intermediate care facilities provide a means to do so. Once patients require >40% oxygen concentrations, mortality risk is significantly increased. COVID-19 continues to place a significant burden of disease on healthcare systems across the globe, and understanding associations with poorer outcomes allows us to mitigate mortality and better manage the pandemic as a whole.

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